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Department of Health Research
Ministry of Health and Family Welfare, Government of India

Standard Treatment Workflow (STW)
MALE INFERTILITY
ICD-11-GB04

WHEN TO SUSPECT?

Inability to conceive even after one year of regular unprotected intercourse.

Evaluation earlier than one year if female age is >35yrs, family history of infertility or very anxious couples.
Infertility incidence is 10-15%.

Prevalence - 180 million couples worldwide and 15% of all couples

*Both have contributory factors in 30-40% cases

Male factor solely responsible in 20% and contributory in 30%

CAUSES

Pretesticular	Testicular	Post testicular
• Hypogonadotrophic hypogonadism, sexual disorders	• Primary testicular failure, cryptorchidism, atrophic testes, testicular tumors, varicocele	• CABVD, EDO, post vasectomy

HOW TO PROCEED?

Both partners examined simultaneously*

Ensure marriage is consummated, couple has frequent timed intercourse with the knowledge of ovulatary cycle

*Male factor is an under recognised problem and the failure to recognise often leads to social and psychological adverse effects. Often the male is evaluated once the female has been examined thoroughly and this delays the treatment . Greater the duration of infertility lesser the chance of success

AIM
- To ascertain contributory male factor
- Identify potentially correctable conditions
- Identify incorrectable condtions that may or may not be amenable to Assisted Reproductive Technique (ART)
- Identify serious underlying medical conditions like pituitary tumors, adrenal tumors, testicular cancer, GUTB, CKD, hypogonadism and other hormonal disorder

PHYSICAL EXAMINATION
- Body habitus (obesity, Klinefelter's). Secondary sexual characters, gynecomastia
- Penis: hypospadias, epispadias chordee
- **Testes:** volume, consistency, masses, contours
- Epididymis: flat, turgid, nodularity. Vas deferens – present/absent thickened or beaded
- Cords-presence of varicocele. Inguinal or scrotal scar
- Rectal examination: cyst, dilated seminal vesicles

HISTORY
- Age of partners and duration of infertility.
- Use of contraception and lubricants.
- Knowledge of ovulation cycle
- Sexual and ejaculatory dysfunction, volume of ejaculate
- Medical illness: STD, diabetes, any febrile illness within last 3 months chronic bronchitis and any debilitating medical condition
- H/o Chemotherapy, Radiotherapy
- Congenital anomalies, cryptorchidism, hypospadias, Chordee
- Testicular torsion, drug history, trauma and swelling
- H/o past surgeries(hernia repair, orchiopexy, retroperitoneal surgery)
- Family history (infertility,consanguinity,genetic disorders)
- Personal history-smoking, tobacco, alcohol, caffeine, drug abuse, anabolic steroids
- Exposure to environmental toxins (pesticides,herbicides, chronic heat and radiation, sauna bath, tight non cotton undergarments, laptops & mobile phone)
- Partner history: Any menstrual abnormality, infertility evaluation till date

INVESTIGATIONS

SEMEN ANALYSIS (ESSENTIAL)
- At least 2 samples 2-4 weeks apart; Abstinence of 1-3 days.; Collected in a sterile, medical grade plastic wide mouth container
- Provided within the lab or transported within an hour at room temperature and examined immediately
- WHO Semen criteria (2021, 6th edition), Volume 1.4 (1.3 - 1.5 mL), Total count 39 (35-40), Total motility 42 % (40-43), Progressive motility 30 % (29-31), Immotile sperms 20% (19-20), Vitality 54% (50-56), Morphology 4% (3.9-4)

DIAGNOSTIC CATEGORIES ACCORDING TO SEMEN ANALYSIS REPORT

Normal Semen Analysis: Rule out sexual dysfunctions, Anatomic abnormalities, Female factor and unexplained

Low volume semen: Incomplete Collection, Retrograde ejaculation, Ejac. duct obstruction, Cong. Absence of VasDeferens, Hypogonadism

- **Azoospermia:** Complete absence of sperm to be confirmed by centrifugation of semen and examining pellet

Obstructive (Epididymal,vasal)
- **Nonobstructive:** (Genetic, Chromosomal, Hormonal, CT/RT, Post torsion testes, orchitis, Cryptorchidism, Idiopathic)
- **Oligo-astheno-teratospermia: Isolated** Asthenospermia: Antisperm antibodies, Sperm structural defect, Hypogonadism
- **Multiple defects:** Varicocele, Cryptorchidism, Genital tract infection, Systemic illness, Prolonged abstinence, Drugs (Sulfasalazine, NFT, Colchicine, Chemotherapy, GnRh analogs, Spironolactone, Ketokonazole, Anabolic steroids, cocaine, alcohol. Chemicals: heavy metals, herbicides, organic solvents, fungicides, pesticides)

Note: If a patient is unable to produce semen consider retrograde ejaculation and anejaculation. Further evaluation may require electro ejaculation or vibrator induced ejaculation

OTHER INVESTIGATIONS
- Extended testing - SDF (sperm DNA fragmentation) test, ROS (reactive oxygen species), Genetic (karyotyping, Y chromosome micro deletion, CFTR mutation in Congenital absence of Vasdeferens)
- Hormonal assay: Serum FSH, LH, Prolactin, Testosterone, Estradiol, T/E ratio
- Culture: Urine, Semen, Prostatic fluid, Antisperm antibodies, Viability assay, Sperm function tests, Scrotal USG & doppler, TRUS, Genetic studies,
- Testicular biopsy (Multiple bilateral biopsies preferably in a center with facility for cryopreservation)

MANAGEMENT

PHC/CHC
- History and Physical examination

Normal Semen report:
(Rule out unconsummation, sexual dysfunction, anatomic abnormailities)
Female partner to be evaluated by gynecologist

Abnormal Semen report:
- Management of reversible nonsurgical causes (Infections etc.) and surgical cause i.e. varicocoele if surgeon available
- Preventive measures: Avoid gonadotoxins, gonadotoxic drugs, smoking, tobacco, chronic heat , excess use of mobiles; Encouraging healthy life style: Nutritious diet, regular physical exercise, avoid stress, use of antioxidants and vitamins(Vit. C, Vit E , Zinc)
- For further evaluation refer to district/ tertiary hospital

DISTRICT HOSPITAL
- Hormonal assay and Testicular biopsy
- Management of sexual and ejaculatory dysfunction
- Management of Varicocele and Hypogonadotropic hypogonadism
- ART: AIH/AID and counselling for adoption

TERTIARY LEVEL
- **Additional testing:** TRUS, Genetic, ASA, SDF, ROS
- **Advanced surgery:** Microsurgical VVA,VEA, Varicocelectomy, TURED, Sperm retreival techniques, Cryopreservation and sperm banking
- **Advanced ART:** IVF-ET/IVF ICSI

TREATMENT ALGORITHM

AZOOSPERMIA
(Low volume, ↓pH, Fructose -ve)

Retrograde ejaculation ruled out

Examine Vas

- Not palpable → CABVD
  - CFTR Gene Mutation → ICSI
  - DI/ Adoption → Counselling
- Palpable → E.D.O. → TRUS
  - Cystic SV & ED → TURED
  - Fibrous → Non-operable → PESA + ICSI

AZOOSPERMIA
(Normal volume, Fructose +ve)

Clinical Examination & FSH

- Obstructive (FSH-N, Epid, turgid) → Normal testes → Exploration, check vasal patency → Needle biopsy (if required) → Microsurgical VEA
- Equivocal (N-FSH, N-testes) → B/L Multiple testicular biopsy
  - Normal → VEA/ ICSI
  - No Sperms → DI/ Adoption
  - Focal Sperms → TESE-ICSI
- P.T.F. (Testes small, FSH>2N) → Discuss options
  - DI/ Adoption
  - Considering ICSI → Genetic study → Multiple testicular biopsy
    - Sperms absent
    - Sperms present → Cryo preservation → ICSI

OLIGO-ASTHENO-TERATOSPERMIA
(↓ count, ↓ motility, poor morphology)

- ↑ FSH, Severe Germ epith damage
- ↑ASA (Role of steroids debatable)
- Varicocele → Varicocelectomy
- Establish Infection → Antibiotics
- Idiopathic → Empirical Medical Rx (Clomiphene, Tamoxifen, HCG, aromatase inhibitors, antioxidants)

→ Refer for Assisted Reproductive Technique (IUI/IVF/ICSI)

NEVER MISS EXAMINING THE MALE PARTNER IN A CASE OF INFERTILE COUPLE

ABBREVIATIONS

AID: Artificial Insemination Donor
AIH: Artificial Insemination Husband
ART: Assited Reproductive Technique
ASA: Anti Sperm Antibodies
CABVD: Congenital Absence of Bilateral Vas deferens
DI: Donor Insemination
EDO: Ejaculatory Duct Obstruction
FSH: Follicle Stimulating Hormone
GUTB: Genito Urinary Tuberculosis
ICSI: Intra Cytoplasmic Sperm Injection
IVF-ET: Invitro Fertiliztion - Embryo Transfer
PESA: Percutaneous Epididymal Sperm Aspiration
PTF: Primary Testicular Failure
SV & ED: Seminal Vesicle & Ejaculatory Duct
TESE: Testicular Sperm Extraction
TRUS: Trans Rectal Ultrasonography
TURED: Trans Urethral Resection of Ejaculatory Duct
VEA: Vasoepididymal Anastomosis
VVA: Vaso Vasostomy

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